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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/914,708

12/20/2001

Michael R. Boyd

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04/19/2006

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EXAMINER

WANG, SHENGJUN

ART UNIT

PAPER NUMBER

1617

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/914,708

Applicant(s)

BOYD, MICHAEL R.

Examiner

Shengjun Wang

Art Unit

1617

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 February 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Receipt of applicants' amendments and remarks submitted February 6, 2006 is acknowledged.

Species Elections

In response to the species election requirements, applicants elected Salicylihalamides A with traverse in the response filed September 17, 2004. Though not specifically stated, the species election requirement was withdrawn, as evidenced by the examination of non-elected species (e.g., claims 6 and 7). On the record, the species election has been withdrawn in response to applicants' traverse.

Claim Rejections 35 U.S.C. 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

2. Claim 1-7 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over McKee et al. (previously referred as McKee et al) (J. Org. Chem., 63, 7805-10) in view of Oku et al. (WO 99/21835) and Simon et al. (2002/0042079).

3. McKee et al. teaches Lobatamindes A-D as having anti-tumor activity. The Lobataminde activity was found to correlate with that of Salicylihalamides A and B because of their common chemical core structures as shown in Figure 3. See, particularly, page 7808, last ¶, to page 7809, first ¶ and page 7810, 8th ¶. McKee et al. et al. does not teach the administration of the apicularen

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A or B, the claimed amounts or the treatment of intra-organellar acidification of intracellular organelles, specifically.

4. Oku et al. teaches malignant tumors (e.g. those related to melanoma and lung cancers) are known to be treatable by vacuolar type H⁺-ATPase inhibition (pp. 15-16).

5. Simon et al. disclose that it is known in the art that the enhanced sensitivity of tumor cells to chemotherapeutics is a consequence of a reduced acidification within the organelles ((0187)).

6. It would have been obvious to one of ordinary skill in the art at the time of the invention to administer a composition of the Lobatamides, Salicylihalamides or Apicularens claimed in a method of treating a tumor because such compounds a core shared by the claimed compounds are taught to be known in the art as anti-tumor agents. Accordingly the skilled artisan would have been motivated to utilize the claimed compounds in a method of treating a tumor because McKee et al. teaches that compounds with such a core are useful therefor.

7. It is noted that while other pathways are possible for the treatment of cancers, such as lung tumors, the administration of the compounds of McKee et al. would obviously meet the claims because Oku et al. teaches that it is known in the art to treat cancers by inhibiting vacuolar type H⁺-ATPase and Simon et al. teaches that it is known in the art to enhance the treatment of cancer by reducing acidification within the organelles. Accordingly, the treatment of, e.g., a lung tumor of McKee et al. would meet the conditions of "A method of treating an intra-organellar acidification of intracellular organelles by the inhibition of vacular-type (H⁺)-ATPase" because a claim for the administration of the same compound to the same population is not rendered patentable by the discovery of a new mechanism by which the treatment works.

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8. It is noted that claims 12-17 are directed to amounts of compound to be administered. It has been established that "where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

9. Claims 8-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over McKee et al., Oku et al. and Simon et al. as applied to claims 1-7, and 12-17 above, and further in view of Holt et al. (WO 93/18652) and Yamamoto et al. (Cell Struct. Funct. 1998, 23, 33-42)

10. McKee et al., Oku et al. and Simon et al. apply as disclosed above. The references lack a teaching of bafilomycins and concanamycins.

11. Holt et al. teaches the administration of bafilomycins (ATPase inhibitors) for the inhibition of cancers (Abstract, p. 2).

12. Yamamoto et al. teaches that the V-ATPase inhibition activity of bafilomycin A1 is related to its cause of autophagy in rat hepatoma cell lines (cancer) (Abstract; pp. 33-34 and 40). Yamamoto et al. also teaches the equivalence of the V-ATPase inhibition activities of bafilomycin A1 and concanamycins (pp. 40-41).

13. It would have been obvious to one of ordinary skill in the art to add the compounds claimed to a treatment of the combined references because Holt et al. teaches bafilomycins as known in the art to be administered for the inhibition of cancer. Furthermore, it would have been obvious to specifically use bafilomycin A₁ as the bafilomycin or to substitute the bafilomycin with concanamycin A in the treatment rendered obvious by McKee et al. and Yamamoto et al. because (1) bafilomycin A1 is a bafilomycin; (2) bafilomycin A1 is taught by Yamamoto et al. to cause autophagy in cancer cells; (3) concanamycins are taught to be the functional equivalent of

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bafilomycin A1 by Yamamoto et al.; and (4) concamamycin A is a concamamycin. "It is prima facie obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Response to the arguments

Applicants' remarks submitted February 6, 2006 have been fully considered, but are not persuasive.

The examiner fully agrees that "The mere fact that an agent may be cytotoxic to cancer cells does not necessarily mean that the mechanism by which the compound is cytotoxic is by the inhibition of vacuolar-type (H⁺)-Atpase, that the compound is able to inhibit vacuolar -type (H⁺)-AtPase or that the compound can be used to treat intra-organellar acidification of intracellular organelles by the inhibition of vacuolar-type (H⁺)-ATPase." However, one of ordinary skill in the art does not need such motivation, or knowledge to reach the obvious method, i.e., treating cancer patient with Lobatamides, or its obvious variation, such as Salicylihalamides or Apicularens. Note Oku et al. and Simon et al. were cited as secondary references showing treating cancer would meet the functional limitation as herein cited. As to Apicularens recited in claims 6 and 7, note since Apicularens share the core structure with Lobatamides, it would have been reasonably expected that they be similarly useful as Lobatamides or Salicylihalamides. See, particularly figure 3 in McKee.

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The instant claims are directed to effecting a biochemical pathway with an old and well known compounds. The argument that such claims are not directed to the old and well known ultimate utility (treating cancer) for the compounds, e.g., Lobatamides, are not probative. It is well settled patent law that mode of action elucidation does not impart patentable moment to otherwise old and obvious subject matter. Applicant's attention is directed to *In re Swinehart*, (169 USPQ 226 at 229) where the Court of Customs and Patent Appeals stated "is elementary that the mere recitation of a newly discovered function or property, inherently possessed by thing in the prior art, does not cause a claim drawn to those things to distinguish over the prior art." Additionally, where the patent Office has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, it possesses the authority to require the applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. In the instant invention, the claims are directed to the ultimate utility set forth in the prior art, albeit distanced by various biochemical intermediates. The ultimate utility for the claimed compounds is old and well known rendering the claimed subject matter obvious to the skilled artisan. The claims as pending fail to distinguish the claimed invention from the old, or otherwise obvious, method. It would follow therefore that the instant claims are properly rejected under 35 USC 103.

14. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO**

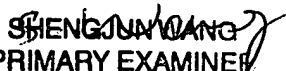
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MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shengjun Wang whose telephone number is (571) 272-0632. The examiner can normally be reached on Monday to Friday from 7:00 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


PRIMARY EXAMINER
Shengjun Wang
Primary Examiner
Art Unit 1617